As an initial matter, the Examiner issued a series of double patenting rejections, first with regard to Claims 1-14, 23, 26 and 29-32 over Claims 1-16 of co-pending application serial no. 09/813,820 and over Claims 1-12 of U.S. Pat. No. 6,288,214. In addition, the present claims were rejected under 35 U.S.C. § 103(a) on the basis of U.S. Pat. No. 6,288,214, which was asserted to be prior art under 35 U.S.C. § 102(e). In all of these cases, the Examiner asserted that because those prior applications disclosed antibodies which bound to regions that included 151-318, e.g., the region covering amino acids of the CNA protein 30-531, these antibodies would inherently recognize the lesser-included 151-318 region. For reasons as explained further below with regard to cited reference WO 97/43314, which is based on the same disclosure as US Pat. 6,288,214 and application 09/813,820, neither of these references ever discloses or suggests the development of antibodies which specifically recognize the CNA19 region as claimed herein, and indeed no prior antibodies raised as disclosed in these cited references exhibited the unexpected cross-reactivity of the antibodies to the CNA19 region as shown in the present application. Accordingly, these references would not anticipate or render the present claims obvious even if considered prior art[1], as explained further below..

In the Official Action, the Examiner rejected the claims under 35 U.S.C. § 112, second paragraph, namely with regard to the use of the term CNA19 peptide and the region 151-318 from the CNA protein binding domain as set forth in Claims 1, 23 and 31. The present amendment now makes minor amendments to these claims to make it clear

[1] Even though there is common ownership between these cases, Applicants thus assert that those references do not affect the patentability of the present claims for the reasons as stated herein.

that what is being referred to by "CNA19" is the peptide in the CNA protein binding domain corresponding to amino acids 151 through 318 of the *S. aureus* CNA protein, the full sequence of which is known and disclosed in prior references. Accordingly, the claims as amended, namely Claims 1 and 23, now make this clear. Finally, the objection to Claim 31 has become moot by virtue of the cancellation of that claim.

In the Official Action, the Examiner rejected Claims 1-14 under 35 U.S.C. § 102(b) as being anticipated by Hook et al. reference WO 97/43314. In addition, as indicated above, the Examiner also consider the present invention to be obvious on the basis of co-pending application 09/813,820 and U.S. Pat. No. 6,288,214 which are in the same patent family as WO 97/43314. For reasons as stated herein and as described further below, these references do not disclose or suggest the present claims.

The Hook references such as WO 97/43314 disclose collagen binding proteins from *Staphylococcus aureus*, as well as antibodies that are generated against this protein and certain identified subregions. Included in the subregions for which antibodies were generated including M17 (corresponding to the subregion at amino acids 151-297 in the collagen binding domain of the CNA protein from *S. aureus),* M31 and M55 (region 30-529). To the contrary, although region 151-318 was identified (se page 3), no antibodies were generated against it, nor was there a suggestion to do so. Indeed, the reference refers to possible truncations that may be necessary, and goes on to disclose the generation of antibodies against M17 (and not CNA19), thus teaching one away from attempting to generate antibodies from the CNA19 region.

It is thus the case that the presently claimed invention, an isolated antibody recognizing the CNA19 region of the *S. aureus* collagen binding protein, is not disclosed or suggested in the cited references. Moreover, the Examiner's rejection appears to be based on the assumption that a lesser included region will generate the same antibodies as will be generated by a larger region which includes the lesser region. In fact, this is not the case. In particular, U.S. Patent 6,288,214 cited by the Examiner is an example of this principle in that an antibody to the M55 region had different properties than, and was considered patentable over, the disclosure of antibodies to the entire CNA protein, of which the M55 region is an included sequence. In short, there can be significant differences between antibodies generated to lesser regions than a larger regions, typically caused by the inclusion or exclusion of specific epitopes which can change significantly the properties of the resulting antibody.

In the present case, the antibodies specific to the CNA19 region of the CNA collagen binding domain of *S. aureus* have now been shown to have the unexpected beneficial property of being cross-reactive to both *S. aureus* and *S. epidermidis,* and thus can be more useful that the prior formulations in that they can provide effective treatment against a wide variety of staphylococcal infections. Accordingly, the present claims are not disclosed or suggested in the cited references, which in fact teach away from the present invention in that they disclose the CNA19 region but do not disclose or suggest raising antibodies against it, and indeed the presently claimed invention gives the beneficial result of cross-reactivity not heretofore disclosed which will improve the efficacy of treatments using these antibodies. Accordingly, the present claims are not

anticipated or made obvious by the Hook references cited by the Examiner, and the rejections on the basis of this reference should be withdrawn.

In the Official Action, the Examiner also rejected claims under 35 U.S.C. §102(b) as being anticipated by the 1995 Patti et al. article. Once again, the Examiner's argument was that this reference disclosed antibodies generated from CNA peptides which inherently must have included the antibody of the invention since the Examiner stated that they inhibited collagen binding. In fact, the 1995 Patti et al. article once again does not disclose or suggest the presently claimed invention, and indeed teaches away from the invention because it again discloses the CNA19 site (region 151-318) but does not disclose or suggest raising antibodies to this region. Instead, the antibodies that were raised were against M17 (region 151-297) and not CNA19 (151-318). See page 12006. The reference clearly does not disclose or suggest obtaining an antibody which would be cross-reactive against *S. aureus* and *S. epidermidis*. Accordingly, this reference does not disclose or suggest the subject matter of the claimed invention and in fact teaches away from the claimed invention and would suggest that one only raise antibodies against a truncated version of CNA19. The 1995 Patti reference thus does not anticipate or make obvious the present claims, and the Examiner's rejection on the basis of this reference should be withdrawn.

Finally, in the Official Action, the Examiner rejected claims under 35 U.S.C. §102(b) as being anticipated by the 1992 Patti et al. article. Once again, the Examiner's argument was that this reference disclosed antibodies generated from the whole CNA protein and thus inherently disclosed the antibody of the presently claimed invention, and

once again this is not the case. As indicated above, an antibody to an entire protein will not be the same as one generated against a particular region within that protein, and in fact the claims of US Pat. No. 6,288,214 directed to an M55 antibody (SEQ ID NO:6) which is a portion of the collagen binding protein were held patentable over the disclosure of an antibody to the entire collagen binding adhesin. In the present case, the antibody of the claimed invention improves upon prior antibodies because it is cross-reactive across different staphylococcal bacteria, and this antibody is not disclosed, either directly or inherently, or suggested in the 1992 Patti et al. paper. Accordingly, the Examiner's rejection on the basis of this reference is respectfully traversed and should be withdrawn.

Applicant thus submits that in light of the present amendments and arguments as set forth above, the present invention is now considered in condition for allowance, and such action is earnestly solicited.

Respectfully submitted,

March 17, 2003

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APPENDIX A

Marked-Up Amended Claims

Please amend the claims as indicated in the following marked-up versions:

B1

1. (Amended) An isolated cross-reactive antibody which recognizes the CNA19 region, amino acids 151-318~~peptide~~ of the collagen binding domain from the *S. aureus* CNA protein.

B2

23. (Amended) An isolated cross-reactive antibody that is generated against the CNA19 region, amino acids 151-318 of the collagen binding domain of the *S. aureus* CNA protein.

31. (Canceled)

32. (Canceled)

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APPENDIX B

Clean Amended Claims

The following is a clean version of the amended claims:

1. (Amended) An isolated cross-reactive antibody which recognizes the CNA19 region, amino acids 151-318 of the collagen binding domain from the *S. aureus* CNA protein.

23. (Amended) An isolated cross-reactive antibody that is generated against the CNA19 region, amino acids 151-318 of the collagen binding domain of the *S. aureus* CNA protein.

31. (Canceled)

32. (Canceled)